REMARKS/ARGUMENTS

The Present Invention

The present invention is directed to a method for treating cancer in a human wherein the cancer is susceptible to treatment with (-)-gossypol, a physiologically acceptable salt of (-)-gossypol, gossypolone, a physiologically acceptable salt of gossypolone, or any combination thereof.

The Pending Claims

Claims 1-30 are currently pending.

Previously Filed Information Disclosure Statements

Applicants request that the Office consider the Information Disclosure Statement dated December 8, 2004 (received by the Office on December 13, 2004), which recites reference "CB", and the Information Disclosure Statement dated December 15, 2004 (received by the Office on December 20, 2004), which recites reference "CC."

Amendments to the Claims

The only amendment to the claims, relative to the previously presented amendments, is to claim 8. Claim 8 has been amended to correct an inadvertent error and maintain consistency throughout the claims. Specifically, the word "pharmaceutically" has been replaced with "physiologically" to modify the phrase "acceptable salt."

The previous claim amendments, originally presented in conjunction with the filing of the reissue application, are as follows. Independent claims 1 and 8 have been amended to recite (-)-gossypol as supported by the specification at, for example, column 7, lines 29-66. Claims 4 and 11 (depending from claims 1 and 8, respectively) have been amended to recite a blood level of "200-1000 ng/dl" of the compounds recited in claims 1 and 8, respectively, as supported by the specification at, for example, column 7, Table 4. New claims 15-30 have been added as supported by the specification at, for example, column 2, lines 20-25, and column 7, lines 29-34. Specifically, claims 15 and 16, depending from claims 1 and 8, respectively, further recite that the cancer is a carcinoid tumor of neuroendocrine tissue located in the lung, pancreas, or gastrointestinal tract. Independent claims 17 and 24 are identical in scope to original claims 2 and 9, respectively, except that claims 17 and 24 further recite that the cancer is a carcinoid tumor of neuroendocrine tissue located in the lung, pancreas, or gastrointestinal tract. Dependent claims 18-23 and 25-30 mirror original claims

2-7 and 9-14, respectively. The amended claims and the newly added claims, therefore, narrow the scope of the originally issued claims.

The Office Action

Claims 1-3, 8-10, 15, and 16 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Band et al. (*Gynecologic Onc.*, 32: 273-277 (1989). Claims 4 and 11-14 have been rejected under 35 U.S.C. § 103 as being unpatentable over Band et al. Claims 5-7 and 17-30 have been indicated as allowable.

Discussion of Rejection Under 35 U.S.C. § 102(b)

Claims 1-3, 8-10, 15, and 16 have been rejected as allegedly anticipated by Band et al. The Office contends that Band et al. discloses that non-reproductive cancer cell lines are sensitive to (-)-gossypol. The Office further contends that the treatment of a carcinoid tumor of neuroendocrine tissue located in the lungs, pancreas, or gastrointestinal tract is inherent from the teachings of Band et al. Applicants respectfully disagree with the Office's latter contention. Applicants point out that the disclosure of Band et al. is directed to *in vitro* testing of racemic gossypol and its (+) and (-) isomers on established cell lines, whereas the claimed methods are directed to the *in vivo* treatment of a cancer in a human.

A single prior art reference must disclose each and every limitation of a claimed invention, either explicitly or inherently, to anticipate the claimed invention. *Mehl/Biophile Int'l Corp. v. Milgraum*, 192 F.3d 1362, 1365, 52 U.S.P.Q.2d 1303, 1305 (Fed. Cir. 1999). Band et al. does not *explicitly* disclose all the limitations of the rejected claims. As a result, the Office relies on the view that Band et al. *inherently* discloses one or more elements of the rejected claims. While the disclosure of a claim limitation can be inherent, rather than explicit, in a reference, the disclosure of limitations in a reference may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient to establish the inherent disclosure of that thing. Inherency must be established as a necessary consequence of what was intended. *Id.* at 1366, 52 U.S.P.Q. at 1305. As succinctly stated in the M.P.E.P., "[i]n relying upon the theory of inherency, the [E]xaminer must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art." M.P.E.P. § 2112 (emphasis added).

The Office has not satisfied the applicable standards for holding that the subject claims are anticipated by the inherent disclosure of Band et al. Band et al. does not anticipate the subject claims explicitly or inherently because Band et al. teaches *in vitro* testing of (-)-gossypol. There is no disclosure of the claimed *in vivo* treatment of a cancer in a human using

(-)-gossypol, and such an *in vivo* treatment is not an inherent result (i.e., an inevitable or necessary consequence) of what is disclosed in Band et al. In other words, by conducting *in vitro* testing in accordance with the disclosure of Band et al., someone would not be doing anything *in vivo*, let alone treating a cancer in a human. The concept of inherency is not even applicable here.

In view of the above, Applicants respectfully request the withdrawal of the Section 102 rejection of claims 1-3, 8-10, 15, and 16.

Moreover, these claims are not properly subject to an obviousness rejection because the claims define subject matter that is unobvious in view of the disclosure of Band et al. In that respect, the Office has not established a correlation between the *in vitro* testing of (-)-gossypol on cell lines as reported in Band et al. and the *in vivo* treatment of a cancer in a human using (-)-gossypol as recited in the rejected claims. Moreover, Band et al. relates to the ability of gossypol to inhibit the proliferation of *both* cancerous and non-cancerous cells *in vitro*. The disclosure of Band et al. demonstrates that gossypol is as lethal to normal, untransformed, non-cancerous cells as it is to cancerous cells. According to the Rule 1.132 Declaration of Dr. Marcus Reidenberg submitted during the prosecution of the patent that is the subject of this reissue application (copy enclosed herewith), "[s]uccessful anticancer drugs *selectively* kill tumor cells; if anticancer drugs killed cells indiscriminately, the cure would be worse than the disease" (paragraph 5 (emphasis in original)). Thus, Band et al. not only fails to provide one of ordinary skill in the art with the motivation to use (-)-gossypol, or any other compound encompassed by the claims, to treat cancer *in vivo*, let alone in a human, Band et al. further fails to provide the artisan of ordinary skill with a reasonable expectation of successful, i.e. safe and effective, treatment. Accordingly, the cancer treatment method defined by claims 1-3, 8-10, 15, and 16 would not have been obvious to one of ordinary skill in the art as of the filing date of the patent that is the subject of this reissue application.

Discussion of Rejection Under 35 U.S.C. § 103

Claims 4 and 11-14 have been rejected under Section 103 as allegedly obvious in view of and, therefore, unpatentable over Band et al. This rejection is traversed for the reasons set forth below.

The Office alleges that claims 4 and 11-14 are obvious in view of Band et al. because a person having ordinary skill in the art would have been motivated to determine the blood concentration of (-)-gossypol with the optimum effectiveness, and to determine an optimum dosage of (-)-gossypol to get the maximum effectiveness.

Applicants note that the Office bears the initial burden of factually supporting any *prima facie* conclusion of obviousness. The appropriate test to establish a *prima facie* case of

obviousness demands that the Office satisfy three requirements: (1) the Office must identify some suggestion or motivation, either in the references relied upon or in the knowledge generally available in the art, to modify the references in such a way as to arrive at the invention claimed, (2) there must be a reasonable expectation of success, and (3) the prior art references relied upon must teach or suggest all of the elements of the claim. *See In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). The Office has not met its burden in establishing a *prima facie* case of obviousness on this basis alone.

First, the Office has not pointed to any teaching or suggestion in Band et al. reference or the relevant art that would render obvious the subject matter of claims 4 and 11-14. The Office merely makes an unsupported conclusion that a person having ordinary skill in the art would have been motivated to identify the optimum blood concentration and dosage of (-)-gossypol, which the Office admits, is not even suggested in Band et al. Although, the motivation to modify a prior art reference can be based on the knowledge generally available in the art at the time the subject application was filed, the Office bears the burden of establishing the level of knowledge generally available in the art at that time. The Office does not point to anything as establishing the level of knowledge in the art at the relevant time as a source of motivation to modify the disclosure of Band et al. Accordingly, the Office has not met its burden in establishing a *prima facie* case of obviousness on this basis alone.

Second, even if the Office had identified some suggestion or motivation in the art to modify Band et al. to arrive at the claimed invention, there was no reasonable expectation that such a modification would be successful. *See* Applicants arguments made against the rejection under 35 U.S.C. § 102(b) *Supra.* As stated above in response to the Section 102 rejection, Band et al. did not establish a correlation between the *in vitro* testing of (-)-gossypol and the *in vivo* efficacy of (-)-gossypol in the treatment of a cancer in a human. *Id.* The Office has not cited to any evidence demonstrating that one of ordinary skill in the art would have reasonably expected the success of the claimed methods in view of the information in the cited references. Although it may have been obvious for a person having ordinary skill in the art to try to treat cancer in a human with (-)-gossypol based on the information in Band et al., "obvious to try" is not the proper standard for evaluating obviousness.

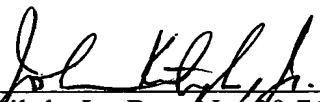
Third, Band et al. does not teach or suggest all of the elements of rejected claims 4 and 11-14. These claims recite the blood concentration and dosage level of (-)-gossypol. These elements of the rejected claims are not disclosed in Band et al. and would not have been readily apparent to one of ordinary skill in the art based on the *in vitro* testing of (-)-gossypol described in Band et al. in view of the significant differences between *in vitro* and *in vivo* environments.

Under the circumstances, the subject matter of claims 4 and 11-14 cannot properly be considered to have been obvious in view of the cited art. Applicants, therefore, request withdrawal of the rejection under Section 103(a).

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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